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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/678,836	10/03/2003	Manoussos Perros	PC10925B	1139

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EXAMINER	
HUANG, EVELYN MEI	
ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 02/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/678,836	PERROS ET AL.	
	Examiner	Art Unit	
	Evelyn Huang	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 38-44 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 38-44 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 38-44 are pending. Claims 1-37 have been canceled according to the preliminary amendment filed on 10-3-2003.

Priority

2. This is a continuation of 09/865950, now US Patent No. 6667314, which claims the priority of Provisional Application No. 60/214587, filed on 6-27-2000, Provisional Application No. 60/219202, filed on 7-19-2000, and UK 0015832.2, filed on 6-27-2000.

The instant application also claims the foreign priority UK 0014046.7, filed on 5-26-2000, which is not claimed in the parent application, 09/865950. The instant application therefore is not a continuation, but rather a CIP of 09/865950.

Clarification is required.

Claim Rejections - 35 USC § 112(2)

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 40, 44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 44, the term 'comprises' in 'modulation comprises' is open-ended and is therefore indefinite.

b. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by

raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 40 recites the broad recitation 'graft rejection', and the claim also recites 'kidney or a lung allograft' which is the narrower statement of the range/limitation.

Claim Rejections - 35 USC § 112(1)

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 38, 44 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant method of treating a disorder in which the modulation of CCR5 receptors is implicated reaches out to as yet unidentified conditions/disorders in which the modulation of CCR5 receptors is implicated, a description of which is not found in the specification.

The term 'modulation' includes agonism and antagonism of the receptors, which embraces different sets of opposing physiological responses, a description of which is not found in the specification. Furthermore, a description of whether the instant compound is an agonist or an antagonist of CCR5 receptor is not found in the specification.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 38-44 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The following evaluation factors have been considered

a. *Nature of the invention.*

The instant invention is drawn to a triazolyl-tropane compound for use in the treatment of a disorder in which modulation of a CCR5 receptor is implicated; the disorders are recited on pages 29-31 of the specification.

b. *State of the prior art and the level of the skill in the art.*

Chemokine receptors exist in several subtypes. While many diseases are implicated to be mediated by the chemokine receptors, the particular responses elicited by each subtype have not been delineated. A substituted aryl-piperazine compound has been described to have binding affinity to the chemokine receptor (Mills, WO 98/25617, PTO-1449). Several small molecule antagonists of chemokine receptor have also been described (Hesselgesser, PTO-1449, page 15689), however, the instant compound does not resemble any of these prior art compounds.

It is well recognized in the art that the binding data do not distinguish the agonists from the antagonists of the chemokine receptor, nor the physiological conditions requiring the activation of an agonist and those requiring the action of an antagonists.

Furthermore, at the time of the invention, there is no umbrella drug known to treat all the diverse diseases as recited in the claims.

The level of the skilled in the chemokine receptor art is high.

c. *Predictability/unpredictability of the art.*

The high degree of unpredictability is well recognized in the chemokine receptor ligand art. A small change in the structure would drastically affect its biological activity as evidenced in the different K_i values for the structurally similar compounds (Hesselgesser, page 15689). Since the in vitro result is highly unpredictable, the degree of unpredictability in the much more complex *in vivo* situation would be expected to be even greater.

d. *Amount of guidance/working examples.*

The preparation of example compounds has been described.

The reference for the procedure for assessing the inhibition of CCR5 binding is found on page 62. The result is described as 'all the tested compounds were found to have an IC_{50} values of less than 10 nM'. No *in vivo* procedures are described.

e. *The breadth of the claims.*

Applicant's assertion that all the inventive compounds would be effective in treating a disorder in which modulation (including agonism and antagonism) of a CCR5 receptor is implicated, and useful in treating diseases of various origins and etiology, including any types of renal diseases, AIDS etc., does not commensurate with the scope of the objective enablement, especially in view of the fact that the binding data does not distinguish an agonist from the antagonist and there is no description of whether the instant compound is an agonist or an antagonist of CCR5 receptor, the existence of a high degree of unpredictability and the absence of working examples directed to specific compounds (paragraphs c, d above).

f. *Quantitation of undue experimentation.*

Since sufficient teaching and guidance have been provided in the disclosure, one of ordinary skill in the art, even with high degree of skill, would not be able to use the all the compound as claimed without undue experimentation, especially when at present, there is no umbrella drug compound that would treat all the diseases as recited in the instant claims.

Conclusion

6. No claims are allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Evelyn Huang whose telephone number is 571-272-0686. The examiner can normally be reached on Tuesday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Evelyn Huang
Primary Examiner
Art Unit 1625